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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
KRISHNAN, GANAPATHY	

ART UNIT	PAPER NUMBER
1623	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/583,760	TREICHLER ET AL.	
	Examiner	Art Unit	
	Ganapathy Krishnan	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 September 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,11,13-21 and 26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6, 11, 13-21 and 26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A Request for Continued Examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed 9/24/2008 has been entered.

The Request for Continued Examination filed 9/24/2008 has been carefully considered. The following information provided in the amendment affects the instant application:

1. Claims 7-10, 12, 22-25 and 27 have been canceled.

2. Claims 1, 13-15, 17-18 and 20-21 have been amended.

3. Remarks drawn to rejections under 35 USC 112, first paragraph and 103(a).

Claims 1-6, 11, 13-21 and 26 are pending in the case.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6, 11, 13-20 and 26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Applicant's amendment has been considered carefully but it is deemed to insert a new matter into the claims as discussed below:

A written description analysis involves three principle factors:

(1) field of the invention

(2) breath of the claims, and

(3) possession of the claimed invention at the time of filing for each claimed species/genus.

The Federal Circuit court stated that written description of an invention "requires a precise definition, such as by structure, formula, or chemical name, of the claimed subject matter sufficient to distinguish it from other material". University of California v. Eli Lilly and Co., 43 USPQ2d 1398 (Fed Cir. 1997). The court also stated "Naming a type of material generally known to exist, in the absence as to what the material consists of is not a definition of that material". Further, the court stated that to adequately describe a claimed genus, adequate must describe a representative number of species of the claimed genus, and that one skilled in the art should be able to "visualize or recognize the identity of the members of the genus".

Field of the invention

The present invention is drawn to cobalamin derivatives of formula I comprising antibiotic and antiproliferative agents, composition of compounds of formula I and method of treatment of a neoplastic disease using compounds of formula I.

Scope and Content of the Claims

Claims 1-6, 11, 13-19 are drawn to compounds of formula I wherein the substituents R^c. R^d and R^e are an antibiotic or antiproliferative therapeutic agent, each connected through a linker

Z, with only one of R^c, R^d, R^e or R^R being hydrogen. This means that if one of R^c, R^d, R^e is hydrogen, the other two should be connected to the therapeutic or antibiotic agent via the linker Z.

Possession of the claimed invention at the time of filing for each claimed species/genus

According to the instant specification (page 8, lines 4-15), only the substituent R^R is an antibiotic or an antiproliferative therapeutic agent connected through the linker Z. *R^c, R^d, R^e is different from hydrogen but is not connected via the linker Z.* Examples 5-25 (page 13-14) and Table 2 (page 28) teach cyanocobalamin derivatives that are not seen to have an antibiotic or an antiproliferative agent attached via a linker. All of the examples have R^c=R^d=R^R = H. A skilled artisan would not be able to envision the genus from just these examples provided. Hence, applicants do not have possession of the invention as instantly claimed. This is a new matter rejection.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 21 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treatment of melanoma, does not reasonably provide enablement for treatment of al other types of cancers as broadly encompassed by the recitation in the instant claim. The specification does not enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

A conclusion of lack of enablement means that, based on the evidence regarding each of the factors below, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation.

(A) The breadth of the claims
(B) The amount of direction provided by the inventor
(C) The existence of working examples
(D) The level of predictability in the art
(E) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The breadth of the claims

The recitation in claim 21, namely, neoplastic disease, is broad and is seen to encompass all types of cancers and tumors and any form not yet known or diagnosed as of the filing date of the instant claims.

The amount of direction provided by the inventor

The specification (page 6) mentions neoplastic diseases such as cancers. This teaching is seen to include all forms of cancer. The CAFC requires a precise definition. One skilled in the art therefore will interpret the terms neoplastic disease/cancers to include all known forms of cancer.

The existence of working examples

The working examples set forth in the instant specification are drawn to therapy studies in mice bearing syngeneic mouse melanoma with ^{188}Re labeled cyanocobalamin derivative. One of ordinary skill in the art will not extrapolate this to methods of treatments using the said

compounds and compositions as instantly claimed to the treatment of all forms of cancer/neoplastic diseases since the examples provided are not representative of all forms of cancer.

The level of Predictability in the Art

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427.2d 833, 166 USPQ (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary to satisfy the statute.

The skilled artisan would view cancers as not treatable with one medicament or therapeutic regimen. Treatment efforts and efforts to cure all cancers have produced only isolated identifiable positive results. See *In re Application of Hozumi et al.*, 226 USPQ 353. Moreover, it is well known that so far no single chemotherapeutic agent has been found to be useful in the treatment of **all** cancers, or even useful in the treatment of all types of breast cancers; and colon cancers; and prostate cancers; and leukemias. For example, breast cancers and leukemia do not share a common cause and differ in their methods of treatment, i.e., breast cancers are routinely with estrogens, antiestrogens, and/or androgens, unlike leukemia which is routinely treated with I-asparaginase, daunorubicin, and purine analogs. It is known that repeated therapeutic failures, after promising in-vitro test results, suggest to the skilled artisan that claims based on in-vitro data, directed to treating cancer generally, are highly unpredictable, as taught in Trisha Gura's article in *Science*, November, 1997:

"[T]he institute started by pulling together mouse models of three tumors: a leukemia, which affects blood cells; a sarcoma, which arise in bone, muscle, or connective tissue; and carcinoma, the most common cells and includes such major killers as breast, colon, and lung cancers.

Initially, many of the agents tested in these models appeared to do well. However, most worked against blood cancers such as leukemia and lymphoma, as opposed to the more common solid tumors. And when tested in human cancer patients, most of these compounds failed to live up to their early promise." (emphasis added, see for example, the middle column of the article).

Based on the known teachings of cancer treatment as in Trisha Gura's reference, one of skill in the art would recognize that it is highly unpredictable in regard to the treatment in the instant case, including treating numerous and various tumors: gynacological tumors, ovarian carcinomas, testicle tumors, prostate carcinomas, skin cancer, kidney cancer, bladder tumors, esophagus carcinomas, stomach cancer, rectal carcinomas, pancreas carcinomas, thyroid cancer, adrenal tumors, various types of leukemia and lymphomas, Hodgkin's disease, tumor illnesses of the CNS, soft-tissue sarcomas, bone sarcomas, benign and malignant mesotheliomas, especially intestine cancer, liver cancer, breast cancer, bronchial and lung carcinomas, melanomas, acute and chronic leukemias and benign papillomatosis tumors, by administering the very same compounds.

The quantity of experimentation needed to make or use the invention based on the content of the disclosure

Indeed, in view of the information set forth, the instant disclosure is not seen to be sufficient to represent method of treatment of all cancers/tumors encompassed by the broad recitation in the instant claim. One of ordinary skill in the art would have to carry out undue experimentation to practice the instant invention. Thus, the specification fails to provide sufficient support of the broad use of the compounds as instantly claimed for treating numerous cancers recited in the instant claims, as a result, necessitating one of skill to perform an

exhaustive search for the embodiment of cancers encompassed by the instant claims suitable to practice the claimed invention.

Genentech, 108 F.3d at 1366, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the *Wands* factor and *In re Fisher* (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in *undue experimentation* to test compounds and tumors/cancers encompassed by the instant claims, with no assurance of success.

Response to Applicants Arguments

The enablement rejection for claims 20-21 under 35 USC 112, first paragraph and the rejection of claims 1-6, 8, 11-21 and 26 under 35 USC 103(a) of record in the previous action have been overcome in view of amendments and applicants' arguments. The rejections under 35 USC 112 as above are being made of record.

Conclusion

Claims 1-6, 11, 13-21 and 26

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathy Krishnan whose telephone number is 571-272-0654. The examiner can normally be reached on 8.30am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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